

5 **SYSTEM AND METHOD FOR ASSESSING CARDIAC PERFORMANCE
THROUGH TRANSCARDIAC IMPEDANCE MONITORING**

Field of the Invention

The present invention relates in general to cardiac performance assessment
and, in particular, to a system and method for assessing cardiac performance
10 through transcardiac impedance monitoring.

Background of the Invention

Heart disease refers to several classes of cardio and cardiovascular
disorders and co-morbidities relating to the heart and blood vessels. Generally,
heart disease is treatable through medication, lifestyle modification and surgical
15 intervention, which involves repairing damaged organs and tissue. Surgical
intervention can also involve implanting active monitoring or therapy delivery
devices, such as pacemakers and defibrillators, and passive intervention means.

Heart disease can lead to heart failure, a potentially fatal condition in
which the heart is unable to supply blood sufficient to meet the metabolic
20 demands of a body. In a clinical setting, cardiac performance, including potential
heart failure, can be detected by measuring changes in arterial blood pressure
immediately before, during and immediately after the performance of
intrathoracic pressure maneuvers, known as dynamic auscultation, which includes
the Valsalva and Müller maneuvers, such as described in Braunwald, "Heart
25 Disease - A Textbook of Cardiovascular Medicine," pp. 46-52 (5th ed. 1997), the
disclosure of which is incorporated by reference.

In particular, potential heart failure can be effectively and safely detected
by evaluating the profile of arterial blood pressure and other cardiac dimensional
measures relative to performance of the Valsalva maneuver, which involves
30 forced expiration against a closed glottis for about 10-30 seconds. In a healthy

person with no prior history of cardiovascular disease or a patient suffering from a diseased but not failed heart, left ventricular ejection fraction (LVEF) and left ventricular end diastolic pressure (LVEDP) change dramatically coincidental to performance of the Valsalva maneuver, whereas LVEF and LVEDP change only slightly in a heart failure patient, as discussed in Hamilton et al., *Arterial, Cerebrospinal and Venous Pressure in Man During Cough and Strain*, 144 Am. J. of Phys., pp. 42, 42-50 (1944) and Zema et al., *Left Ventricular Dysfunction – Bedside Valsalva Maneuver*, Br. Heart J., pp. 44:560-569 (1980), the disclosures of which are incorporated by reference.

10 Circulatory effects and arterial blood pressure profile undergo four well-documented phases during performance of the Valsalva maneuver. During Phase I (initial strain), systemic arterial pressure increases approximately equal to the increase in intrathoracic pressure. During Phase II (strain duration and cessation of breathing), pulse pressure narrows and systemic systolic pressure decreases.

15 During Phase III (strain discontinuation and resumption of normal breathing), systolic pressure drops rapidly. During Phase IV (recovery), diastolic and systolic pressures overshoot and return to pre-maneuver levels. The four phases form a characteristic signature and periodic analysis of arterial blood pressure profile or blood pressure, specifically LVEF and LVEDP, throughout each phase can be

20 indicative of the patient's heart failure status.

 Regularly obtaining and evaluating LVEF and LVEDP for cardiac performance assessment, however, can be difficult. Direct measurements can be obtained through catheterization and electrodes. LVEF and LVEDP can be measured directly through a catheter distally placed into the left ventricle, but the

25 procedure is invasive and creates unfavorable risks. Pulmonary artery wedge pressure (PAWP), measured through right heart catheterization, can be used as a surrogate measure for LVEDP, but the procedure is also invasive and risky. Moreover, catheterization is impractical in a non-clinical setting. Finally, chronically implanted cardiac pressure electrodes, while less risky, are generally

30 inaccurate and unreliable. Consequently, indirect measurements approximating LVEF and LVEDP are preferable.

For example, intracardiac impedance is readily measured through cardiac impedance plethysmography and can be used as an indirect measure of LVEF and LVEDP. Changes in intracardiac impedance correlate to cardiac dimensional changes, such as described in McKay et al., *Instantaneous Measurement of Left and Right Ventricular Stroke Volume and Pressure-Volume Relationships with an Impedance Catheter*, Circ. 69, No. 4, pp. 703-710 (1984), the disclosure of which is incorporated by reference. As a result, by measuring intracardiac impedance, a profile of LVEDP and LVEF response during performance of the Valsalva maneuver can be obtained indirectly without resorting to invasive direct measurement techniques. Known plethysmography techniques for indirectly measuring intracardiac impedance, however, adapt poorly to effective long-term monitoring.

U.S. Patent No. 4,548,211 to Marks discloses the use of external admittance impedance plethysmography to measure pulsatile volume and net inflow in a limb or body segment. External electrodes are placed on the skin and a voltage is applied and sensed for use in determining absolute physiologic values of peak-to-peak pulsatile volume and peak net inflow. While instrumental in non-invasively measuring peripheral blood flow dynamics, the Marks device fails to measure or monitor cardiac dimensional changes through intracardiac impedance.

U.S. Patent No. 5,788,643 to Feldman discloses a process for monitoring patients with chronic congestive heart failure (CHF) by applying a high frequency current between electrodes placed on the limbs of a patient. Current, voltage and phase angle are measured to calculate resistance, reactance, impedance, total body water and extracellular water, which are compared to a baseline for identifying conditions relating to CHF. The Feldman process is limited to operating on external peripheral electrodes and fails to measure or monitor cardiac dimensional changes through intracardiac impedance.

U.S. Patent Nos. 6,120,442 and 6,238,349 both to Hickey disclose an apparatus and method for non-invasively determining cardiac performance parameters, including systolic time intervals, contractility indices, pulse amplitude ratios while performing the Valsalva maneuver, cardiac output indices, and pulse

wave velocity indices. A catheter is inserted into the esophagus and a balloon is pressurized at a distal end, positioned adjacent to the aortic arch to sense aortic pressure. The affects of aortic pressure on the balloon are utilized to determine the cardiac performance parameters. The Hickey devices, while capable of
5 assessing cardiac performance, must be performed in a clinical setting and fails to measure or monitor cardiac dimensional changes through intracardiac impedance.

U.S. Patent Nos. 3,776,221 and 5,291,895 both to McIntyre disclose a pressure-sensing device for providing a signal representative of systemic arterial blood pressure before and after performance of the Valsalva maneuver.
10 Specifically, an electrode placed on the skin generates a blood pressure signal and measures changes in amplitude before and after the Valsalva maneuver is performed. The McIntyre devices are limited to operating with external skin electrodes and fail to measure or monitor cardiac dimensional changes through intracardiac impedance.

15 Therefore, there is a need for an approach to assessing cardiac performance by indirectly measuring arterial blood pressure profile through intracardiac impedance relative to performance of intrathoracic pressure maneuvers, such as the Valsalva maneuver. Preferably, such an approach would analyze an intrathoracic pressure maneuver signature in a non-clinical setting on a
20 regular basis for use in automated heart disease patient management.

Summary of the Invention

A system and method for generating a cardiac performance assessment based on intracardiac impedance is described. Intracardiac impedance measures are collected during the induced performance of an intrathoracic pressure
25 maneuver, such as the Valsalva maneuver, using an implantable cardiac device. The start of the intrathoracic pressure maneuver is either expressly marked by the patient or implicitly derived by the implantable cardiac device or by an intrathoracic pressure sensing device. The collected intracardiac impedance measures are periodically evaluated for determining arterial blood pressure
30 profile. The intracardiac impedance measures are correlated to arterial blood pressure and assigned to the respective phases of the Valsalva maneuver, if

applicable. A arterial blood pressure profile trend determined for each of the phases is evaluated and the overall set of trends is compared to the signature characteristic of the intrathoracic pressure maneuver under consideration. A cardiac performance assessment is generated based on the closeness of match to the characteristic signature and a notification is generated if the cardiac performance assessment varies beyond a set of predefined thresholds.

An embodiment provides a system and method for evaluating cardiac performance relative to performance of an intrathoracic pressure maneuver. Blood pressure is indirectly sensed by directly collecting intracardiac impedance measures through an implantable medical device. Cardiac functional changes to the blood pressure are evaluated in response to performance of an intrathoracic pressure maneuver.

A further embodiment provides a system and method for assessing cardiac performance through transcardiac impedance monitoring. Intracardiac impedance measures are directly collected through an implantable medical device. The intracardiac impedance measures are correlated to cardiac dimensional measures relative to performance of an intrathoracic pressure maneuver. The cardiac dimensional measures are grouped into at least one measures set corresponding to a temporal phase of the intrathoracic pressure maneuver. The at least one cardiac dimensional measures set is evaluated against a cardiac dimensional trend for the corresponding intrathoracic pressure maneuver temporal phase to represent cardiac performance.

Still other embodiments of the present invention will become readily apparent to those skilled in the art from the following detailed description, wherein are described embodiments of the invention by way of illustrating the best mode contemplated for carrying out the invention. As will be realized, the invention is capable of other and different embodiments and its several details are capable of modifications in various obvious respects, all without departing from the spirit and the scope of the present invention. Accordingly, the drawings and detailed description are to be regarded as illustrative in nature and not as restrictive.

Brief Description of the Drawings

FIGURE 1 is a schematic diagram showing an implantable medical device monitoring transcardiac impedance, in accordance with a further embodiment of the present invention.

5 FIGURE 2 is a schematic diagram showing an external medical device assisting in monitoring transcardiac impedance, in accordance with a further embodiment of the present invention.

FIGURES 3A-C are graphical representations showing, by way of example, averaged arterial blood pressure profiles relative to performance of the Valsalva maneuver in a healthy person, a patient suffering from heart disease and
10 a patient suffering from heart failure.

FIGURE 4 is a graphical representations showing, by way of example, cardiac dimension profiles during diastole and systole, respectively, relative to performance of the Valsalva maneuver in a healthy person, a patient suffering
15 from heart disease but not significant heart failure and a patient suffering from significant heart failure.

FIGURE 5 is a graphical representations showing, by way of example, stroke volume index profile and left ventricular pressure profile relative to performance of the Valsalva maneuver in a healthy person.

20 FIGURE 6 is a functional block diagram showing a system for assessing cardiac performance through transcardiac impedance monitoring, in accordance with a further embodiment of the present invention.

FIGURE 7 is a graphical representation showing, by way of example, trend analysis of arterial blood pressure profile.

25 FIGURE 8 is a graphical representations showing, by way of example, trend analysis of cardiac stroke volume profile.

FIGURE 9 is a flow chart showing a method for assessing cardiac performance through transcardiac impedance monitoring, in accordance with a further embodiment of the present invention.

30 FIGURE 10 is a flow chart showing a routine for collecting physiological measures for use in the method of FIGURE 9.

FIGURE 11 is a flow chart showing a routine for assessing cardiac performance for use in the method of FIGURE 9.

FIGURE 12 is a flow chart showing a routine for evaluating cardiac stroke volume profile relative to, by way of example, the Valsalva maneuver, for use in
5 the routine of FIGURE 11.

Detailed Description

Internal Transcardiac Impedance Monitoring System

FIGURE 1 is a schematic diagram 100 showing an implantable medical device (IMD) 103 monitoring transcardiac impedance, in accordance with a
10 further embodiment of the present invention. The IMD 103 is surgically implanted in the chest or abdomen of a patient and consists generally of a housing 104 and terminal block 105. The IMD 103 is coupled to a set of leads 106a-b at the terminal block 105. During surgery, the leads 106a-b are threaded through a vein and placed into the heart 102 with the distal tips of each lead 106a-b
15 positioned in direct contact with tissue inside the heart 102.

The housing 104 contains a battery 107, control circuitry 108, memory 109, and telemetry circuitry 110. The battery 107 provides a finite power source for the IMD components. The control circuitry 108 samples and processes raw data signals and includes signal filters and amplifiers, memory and a
20 microprocessor-based controller, as would be appreciated by one skilled in the art. The memory 109 includes a short-term, volatile memory store in which raw physiological signals can be stored as telemetered signals for later retrieval and analysis. The telemetry circuitry 110 provides an interface between the IMD 103 and external devices (not shown). The telemetry circuitry 110 enables operating
25 parameters to be non-invasively programmed into the memory 109 through an external device in telemetric communication with the IMD 103. The telemetry circuitry 110 also allows patient information collected by the IMD 103 and transiently stored in the memory 109 to be sent to the external device for processing and analysis.

The IMD 103 is in direct electrical communication with the heart 102 through electrodes 111a-b positioned on the distal tips of each lead 106a-b. By way of example, the set of leads 106a-b can include a right ventricular electrode 111a and a right atrial electrode 111b. The right ventricular electrode 111a is
5 preferably placed in the right ventricular apex 112 of the heart 102 and the right atrial electrode 111b is preferably placed in the right atrial chamber 113 of the heart 102. The electrodes 111a-b enable the IMD 103 to directly collect raw physiological measures, preferably through millivolt measurements. Other configurations and arrangements of leads and electrodes, including the use of
10 single and multiple leads arrays and single and multiple electrodes, can be used, as would be recognized by one skilled in the art.

In the described embodiment, the IMD 103 can be implemented as part of cardiac pacemakers used for managing bradycardia, implantable cardioverter defibrillators (IMDs) used for treating tachycardia, and other types of implantable
15 cardiovascular monitors and therapeutic devices used for monitoring and treating heart failure, structural problems of the heart, such as congestive heart failure, rhythm problems, and other heart conditions, as would be appreciated by one skilled in the art. Examples of cardiac pacemakers suitable for use in the described embodiment include the Pulsar Max II, Discovery, and Discovery II
20 pacing systems, sold by Guidant Corporation, St. Paul, MN. An example of an IMD suitable for use in the described embodiment includes the Contak Renewal cardiac resynchronization therapy defibrillator, also sold by Guidant Corporation, St. Paul, Minn.

On a regular basis, the telemetered signals stored in the memory 109 are
25 retrieved. By way of example, a programmer (not shown) can be used to retrieve the telemetered signals. However, any form of programmer, interrogator, recorder, monitor, or telemetered signals transceiver suitable for communicating with IMD 103 could be used, as would be appreciated by one skilled in the art. In addition, a server, personal computer or digital data processor could be interfaced
30 to the IMD 103, either directly or via a telemetered signals transceiver configured to communicate with the implantable medical device 103.

The programmer communicates with the IMD 103 via radio frequency signals exchanged through a wand placed over the location of the IMD 103. Programming or interrogating instructions are sent to the IMD 103 and the stored telemetered signals are downloaded into the programmer. Once downloaded, the
5 telemetered signals can be sent via a network, such as the Internet, to a server (not shown), which periodically receives and stores the telemetered signals in a database, as further described below with reference to FIGURE 6.

An example of a programmer suitable for use in the present invention is the Model 2901 Programmer Recorder Monitor, manufactured by Guidant
10 Corporation, Indianapolis, IN, which includes the capability to store retrieved telemetered signals on a proprietary removable floppy diskette. The telemetered signals could later be electronically transferred using a personal computer or similar processing device, as would be appreciated by one skilled in the art.

Other alternate telemetered signals transfer means could also be employed.
15 For instance, the stored telemetered signals could be retrieved from the IMD 103 and electronically transferred to a network using a combination of a remote external programmer and analyzer and a remote telephonic communicator, such as described in U.S. Patent No. 5,113,869, the disclosure of which is incorporated by reference. Similarly, the stored telemetered signals could be retrieved and
20 remotely downloaded to a server using a world-wide patient location and data telemetry system, such as described in U.S. Patent No. 5,752,976, the disclosure of which is incorporated herein by reference.

Externally-Assisted Transcardiac Impedance Monitoring System

FIGURE 2 is a schematic diagram 120 showing an external medical
25 device 122 assisting in monitoring transcardiac impedance, in accordance with a further embodiment of the present invention. The external medical device 122 facilitates transcardiac impedance monitoring by ensuring consistent intrathoracic pressure, particularly when thoracic pressure is elevated when induced, for instance, by performance of the Valsava maneuver. The external medical device
30 122 includes a mouthpiece 123 functionally connected to a pressure monitor 124 via a hose 125. The pressure monitor 124 defines a confined volume into which

the patient 121 blows. A pressure regulating device 126 releases expired air. The pressure monitor 124 provides a pressure reading representative of the pressure in the confined volume. The pressure monitor 124 can also provide recording functions that record the pressure levels during performance of a transcatheter maneuver by a patient 121.

In a further embodiment, a thoracic pressure electrode, such as described in U.S. Patent No. 6,132,384, the disclosure of which is incorporated by reference, can be combined with the IMD 103 to provide a fully implanted solution. The use of an implanted thoracic pressure electrode enables measurements during normal activities of daily living that produce elevated thoracic pressure similar to an induced performance of the Valsalva maneuver. When an elevated thoracic pressure is detected by the implanted thoracic pressure electrode, intracardiac impedance is recorded by the IMD 103 on a continuous basis. After the cardiac response period ends, the recorded intracardiac impedance data can either be downloaded to an external device (not shown) for further analysis, as further described below with reference to FIGURE 11, or can be analyzed by the IMD 103.

Arterial Blood Pressure Profiles

FIGURES 3A-C are graphical representations showing, by way of example, averaged arterial blood pressure profiles 130, 150, 170 relative to performance of the Valsalva maneuver in a healthy person, a patient suffering from heart disease but not significant heart failure and a patient suffering from significant heart failure, respectively. The x-axis 131, 151, 171 respectively represent time. The y-axis 132, 152, 172 respectively indicate arterial pressure (mmHg). Averaged changes in arterial pressure are plotted over time throughout each of the four phases 133-136, 153-156, 173-176 of the Valsalva maneuver, respectively. For clarity, the pulsatile arterial blood pressure changes are shown as averaged values and each of the averaged arterial blood pressure profiles 130, 150, 170 have respectively been normalized relative to time.

The Valsalva maneuver involves deep inspiration followed by forced exhalation against a closed glottis for ten to twelve seconds. The four phases of

the Valsalva maneuver exhibit a characteristic signature for normal healthy people and for patients suffering from heart disease, but not significant heart failure.

During Phase I, initial strain, systemic blood pressure undergoes a transient rise as straining commences. During Phase II, strain duration and cessation of breathing,

5 systemic venous return, blood pressure and pulse pressure decrease perceptibly.

During Phase III, strain discontinuation and resumption of normal breathing, blood pressure and systemic venous return exhibit abrupt, transient decreases.

During Phase IV, recovery, systemic arterial pressure overshoots with reflex bradycardia. However, for patients suffering from heart failure, the response

10 signature is a muted square wave response with a slight elevation in blood pressure during phase III and minimal perceptible changes during Phases I, II and IV.

Cardiac performance response profile is significantly dependent on left ventricular function, specifically LVEF and mean LVEDP. A healthy person with

15 no history of cardiovascular diseases may, for example, be expected to have an LVEF and mean LVEDP of approximately 70% and 14 mmHg, respectively. A

patient suffering from heart disease but not significant heart failure may, for example, typically be expected to have an LVEF and mean LVEDP of approximately 50% and 20 mmHg, respectively. A patient suffering from heart

20 failure may, for example, typically be expected to have an LVEF and mean LVEDP of approximately 30% and 40 mmHg, respectively..

Healthy Person

Referring first to FIGURE 3A, the graphical representation shows, by way of example, an averaged arterial blood pressure profile 130 relative to

25 performance of the Valsalva maneuver in a healthy person with no history of cardiovascular diseases. During Phase I 133, intrathoracic pressure increases in response to the strain associated with the maneuver, along with a sharp rise 137 in arterial pressure approximately equal to the intrathoracic pressure increase.

During Phase II 134, pulse pressure narrows and arterial pressure undergoes a

30 transient decrease 138. During Phase III 135, systolic pressure drops rapidly 139.

Finally, during Phase IV 136, diastolic and systolic pressures return to pre-manuever levels 141 following a large overshoot 140 in arterial pressure.

Patient Suffering from Heart Disease But Not Significant Heart Failure

Referring next to FIGURE 3B, the graphical representation shows, by way of example, an averaged arterial blood pressure profile 150 relative to performance of the Valsalva maneuver in a patient suffering from heart disease but not significant heart failure. During Phase I 153, systemic arterial pressure increases only slightly 157. During Phase II 154, systemic arterial pressure 158 increases approximately equal to the increase in intrathoracic pressure followed by a narrowing of pulse pressure and arterial pressure decrease 159. During Phase III 155, systolic pressure drops rapidly 160. Finally, during Phase IV 156, diastolic and systolic pressures return to pre-manuever levels 161 without overshoot.

Patient Suffering from Heart Failure

Finally, referring first to FIGURE 3C, the graphical representation shows, by way of example, an averaged arterial blood pressure profile 170 relative to performance of the Valsalva maneuver in a patient suffering from heart failure. During Phase I 173, almost no appreciable increase in systemic arterial pressure occurs 177. During Phase II 174, pulse pressure and systemic systolic pressure remain at approximately the same elevated level 178 throughout the phase. During Phase III 175, systolic pressure decreases to approximately the same level as in Phase I 173. During Phase IV 176, diastolic and systolic pressures return to their pre-manuever levels 180 almost immediately upon cessation of strain.

Cardiac Dimension Profiles

FIGURE 4 is a graphical representations showing, by way of example, cardiac dimension profiles 182a, 182b, during diastole and systole, respectively, relative to performance of the Valsalva maneuver in a healthy person, a patient suffering from heart disease but not significant heart failure and a patient suffering from significant heart failure. The x-axis represents time. The y-axis

indicates average dimensional change (%). Averaged changes in dimension are plotted over time throughout each of the four phases 183a-186a, 183b-186b of the Valsalva maneuver.

Healthy Person

5 During Phase I 183a, 183b, cardiac dimension decreases in response to the strain associated with the maneuver for a healthy person with no history of cardiovascular diseases. During Phase II 184a, 184b, cardiac dimension reduces rapidly. During Phase III 185a, 185b, cardiac dimension increases rapidly. Finally, during Phase IV 186a, 186b, cardiac dimension pressures return to pre-
10 maneuver levels.

Patient Suffering from Heart Disease But Not Significant Heart Failure

The average cardiac dimensional change for a patient suffering from heart disease but not significant heart failure 182ab, 182bb, is essentially the same as the changes observed for a healthy person with no history of cardiovascular
15 diseases.

Patient Suffering from Heart Failure

The average cardiac dimensional change for a patient suffering from significant heart failure reflects only slight changes during each of the four phases of a Valsalva maneuver.

20 Stroke Volume and Left Ventricular Pressure Profiles

FIGURE 5 is a graphical representations showing, by way of example, stroke volume index profile 188a and left ventricular pressure profile 188b relative to performance of the Valsalva maneuver in a healthy person. The x-axis represents time. The left hand y-axis indicates stroke volume index (ml/M^2) and
25 the right hand y-axis indicates LV pressure. Changes in stroke volume index and left ventricular pressure are plotted over time throughout each of the four phases 187a, 187b, 187c and 187d of a Valsalva maneuver. During Phase I 187a, the stroke volume index decreases slightly and left ventricular systolic and diastolic pressures increase slightly. During Phase II 187b, the stroke volume index and

left ventricular and diastolic pressures decrease significantly. During Phase III 187c, the stroke volume index begins an increase towards pre-maneuver levels, but the left ventricular diastolic and systolic pressures remain stable. Finally, during Phase IV 187d, the stroke volume index and left ventricular diastolic and systolic pressures return to pre-maneuver levels.

LVEF and LVEDP Correlations

Heart disease patient management requires carefully monitoring and evaluation of LVEF and LVEDP. In heart failure patients, an increase in LVEDP can lead to an acute exasperation of heart failure and acute decompensation. Changes to LVEDP associated with the acute exasperation of heart failure can occur in a few days, whereas changes to LVEF occur more slowly and are associated with long-term changes. Thus, effectively assessing cardiac performance, particularly for heart disease and heart failure patients, requires evaluating LVEF and LVEDP or equivalent values that approximate LVEF and LVEDP changes, such as intracardiac impedance.

Comparing the averaged cardiac dimension profiles 182a, 182b described above with reference to FIGURE 4, healthy people and patients suffering from heart disease undergo significant dimensional changes during performance of the Valsalva maneuver, while the cardiac dimensions in patients with significant heart failure changes only slightly. Intracardiac impedance has been empirically correlated to changes in left ventricular pressure, such as described in Wortel et al., *Impedance Measurements in the Human Right Ventricular Using a New Pacing System*, Pacing Clinical Electrophysiology, Vol. 14(9), pp. 1336-42 (Sept. 1991), the disclosure of which is incorporated by reference, and can therefore be used as a surrogate measure of cardiac dimensional changes.

In a further embodiment, the Müller maneuver is performed either in lieu of or in addition to the Valsalva maneuver. The Müller maneuver involves deep inspiration while the nose is held closed and mouth firmly sealed for ten seconds. The Müller maneuver exaggerates inspiration effort and augments murmurs and right side cardiac filling sounds.

System Modules

FIGURE 6 is a functional block diagram showing a system 190 for assessing cardiac performance through transcardiac impedance monitoring, in accordance with a further embodiment of the present invention. Each component
5 is a computer program, procedure or process written as source code in a conventional programming language, such as the C++ programming language, and is presented for execution by one or more CPUs as object or byte code in a uniprocessing, distributed or parallelized configuration, as would be appreciated by one skilled in the art. The various implementations of the source code and
10 object and byte codes can be held on a computer-readable storage medium or embodied on a transmission medium in a carrier wave.

The system 190 consists of a server 191 coupled to a database 197, which provides persistent secondary storage. The server 191 consists of three modules: telemetry 192, database 193, and analysis 194. The telemetry module 192
15 communicatively interfaces to the IMD 103 through a logically-formed, non-invasive communication channel, such as provided through induction, static magnetic field coupling, or by related means, as would be appreciated by one skilled in the art. The telemetry module 192 facilitates the transferal and exchange of physiological measures 195 and programming parameters 196 between the
20 IMD 103 and the server 191. The physiological measures 195 include raw physiological data regularly collected by the IMD 103 and stored in the memory 109. The programming parameters 196 include monitoring and therapy delivery device configuration settings, which are exchanged between the IMD 103 and the server 191. The telemetry module 192 communicates with the telemetry circuitry
25 110 on the IMD 103 using standard programmer communication protocols, as would be appreciated by one skilled in the art.

For an exemplary cardiac implantable medical device, the physiological measures 195 and programming parameters 196 non-exclusively present patient information recorded on a per heartbeat, binned average or derived basis and
30 relating to atrial electrical activity, ventricular electrical activity, minute ventilation, patient activity score, cardiac output score, mixed venous oxygenation

score, cardiovascular pressure measures, time of day, the number and types of interventions made, and the relative success of any interventions, plus the status of the batteries and programmed settings.

5 The database module 193 maintains information stored in the database 197 as structured records for facilitating efficient storage and retrieval. The database module 193 stores the physiological measures 195 and programming parameters 196 exchanged with the IMD 103 in the database 197. The database 197 stores the physiological measures 195 as derived measures, which include, non-exclusively, impedance measures 198, cardiac dimensional measures 199, LVEF measures 10 200, and LVEDP measures 201. Other raw and derived measures can be stored in the database 197, as would be recognized by one skilled in the art. The programming parameters 196 are maintained in the database as programming values 202. In addition, patient profile information 203 is maintained in the database 197.

15 The analysis module 194 derives and evaluates the physiological data maintained in the database 197. As necessary, the physiological measures 195 retrieved from the IMD 103 are converted and derived into the impedance measures 198, cardiac dimensional measures 199, LVEF measures 200, and LVEDP 201, as would be appreciated by one skilled in the art. In particular, the 20 impedance measures 198 are analyzed and evaluated to determine an overall arterial blood pressure profile, which is compared to predefined thresholds 204 for assessing cardiac performance relative to the performance of an intrathoracic pressure maneuver, as further described below with reference to FIGURE 11. The analysis module 194 generates a cardiac performance assessment 205, which 25 identifies trends indicating cardiovascular disease and, in particular, heart failure, absence, onset, progression, regression, and status quo. The cardiac performance assessment 205 can be further evaluated to determine whether medical intervention is necessary.

30 In a further embodiment, the functions of the server 191 are performed by the IMD 103, which directly generates the cardiac performance assessment 205, for retrieval by an external device.

Arterial Blood Pressure Profile Trend Analysis

FIGURE 7 is a graphical representation showing, by way of example, trend analysis 210 of arterial blood pressure profile 213. The *x*-axis 211 represents time. The *y*-axis 212 indicates arterial pressure in mmHg. Averaged changes in arterial pressure are plotted over time throughout each of the four phases 214-217 of the Valsalva maneuver.

The arterial blood pressure profile 213 models the characteristic signature exhibited during each phase of the Valsalva maneuver. During Phase I 214, the arterial pressure is evaluated for an increasing trend 218. During Phase II 215, the arterial pressure is evaluated for a transient decreasing trend 219. During Phase III 216, the arterial pressure is evaluated for a significantly decreasing trend 220. Finally, during Phase VI 217, the arterial pressure is evaluated for a steeply increasing trend 221, followed by an overshooting trend 222, followed by a decreasing trend 223 with resumption of normal arterial pressure. In addition to the arterial pressure trends 218-223, pulsatile volume and heart rate can also be evaluated for trends, as would be recognized by one skilled in the art.

Cardiac Stroke Volume Profile Trend Analysis

FIGURE 8 is a graphical representation showing, by way of example, trend analysis 213 of cardiac stroke volume profile. The *x*-axis represents time. The *y*-axis indicates stroke volume index in ml/M². Averaged changes in stroke volume index are plotted over time throughout each of four phases 214, 215, 216, 217 of a Valsalva maneuver.

Transcardiac Impedance Monitoring Method

FIGURE 9 is a flow chart showing a method 225 for assessing cardiac performance through transcardiac impedance monitoring, in accordance with a further embodiment of the present invention. The method 225 is described as a sequence of process operations or steps, which can be executed, for instance, by a server 191 (shown in FIGURE 6). In a further embodiment, the method 225 can be executed directly by the IMD 103 or related means, which generates a cardiac performance assessment 205 for retrieval by an external device.

The method 225 preferably executes as a continuous processing loop 226-229. During each iteration (block 226), the physiological measures 195 are retrieved from the IMD 103 and stored in the database 197, as further described below with reference to FIGURE 10. Cardiac performance is then assessed (block 228), as further described below with reference to FIGURE 11. Processing continues (block 229), until the method exits or terminates.

Collecting Physiological Measures

FIGURE 10 is a flow chart showing a routine 230 for collecting physiological measures for use in the method 225 of FIGURE 9. The purpose of this routine is to regularly interface to the IMD 103, retrieve the physiological measures 195 and programming parameters 196, and store the retrieved physiological measures 195 and programming parameters 196 in the database 197.

The routine begins initially by interfacing to the IMD 103 (block 231), using, for instance, inductive or static magnetic means, as would be appreciated by one skilled in the art. Raw physiological measures 195 are retrieved from the IMD 103 (block 232). The raw physiological measures 195 are converted and derived into impedance measures 198, cardiac dimensional measures 199, LVEF measures 200, and LVEDP measures 201 (block 233). The physiological measures are stored in the database 197 (block 234). If further physiological measures 195 or programming parameters 196 require exchange with the IMD 103 (block 235), processing continues. Otherwise, the interface to the IMD 103 is closed (block 236), the routine returns.

Assessing Cardiac Performance

FIGURE 11 is a flow chart showing a routine 240 for assessing cardiac performance for use in the method 225 of FIGURE 9. The purpose of this routine is to periodically assess cardiac performance through an analysis of the cardiac stroke volume profile trends 224 (shown in FIGURE 8).

As an initial step, physiological measures, including impedance measures 198, cardiac dimensional measures 199, LVEF measures 200, and LVEDP

measures 201, are retrieved from the database 197 (shown in FIGURE 6) (block 241). The start of the intrathoracic pressure maneuver under consideration is determined (block 242). In the described embodiment, the start of the intrathoracic pressure maneuver is determined by retrieving an explicit marker
5 recorded by the patient 100 or by indirect means based upon an analysis of the retrieved physiological measures, as would be appreciated by one skilled in the art.

Next, the cardiac stroke volume profile 224 is evaluated to form a cardiac performance assessment 205 (block 243), further described below with reference
10 to FIGURE 12. If the cardiac performance assessment 205 exceeds the predefined threshold 204 (block 244), a notification is generated (block 245). In the described embodiment, the notification takes the form of generating an alert for review and possible action by healthcare providers and can include generating appropriate feedback to the patient 100, such as described in commonly-assigned U.S. Patent
15 No. 6,203,495, the disclosure of which is incorporated by reference.

If the cardiac performance assessment 205 does not exceed the threshold 204 (block 244), no notification is generated. If further retrieved physiological measures require evaluation (block 246), processing continues. Otherwise, the routine returns.

20 Evaluating Arterial Blood Pressure Profile Relative to Valsalva Maneuver

FIGURE 12 is a flow chart showing a routine 250 for evaluating cardiac stroke volume profile 224 relative to, by way of example, the Valsalva maneuver, for use in the routine 240 of FIGURE 11. The purpose of this routine is to generate a cardiac performance assessment 205 by forming a trend analysis of the
25 retrieved physiological measures based on the phases of the Valsalva maneuver.

The trend analysis proceeds in four groups of steps (blocks 251-253, 254-256, 257-259, 260-268, respectively), which track each of the four phases of the Valsalva maneuver. During the first group, if the cardiac stroke volume profile 224 is in Phase I (block 251) and an increase in arterial pressure is apparent
30 (block 252), the increase is marked (block 253). During the second group, if the cardiac stroke volume profile 224 is in Phase II (block 254) and a transient

decrease in arterial pressure is apparent (block 255), the transient decrease is marked (block 256). During the third group, if the cardiac stroke volume profile 224 is in Phase III (block 256) and a significant decrease in arterial pressure is apparent (block 258), the significant decrease is marked (block 259). Finally, 5 during the fourth group, if the cardiac stroke volume profile 224 is in Phase VI (block 260), four conditions are evaluated. If an increase in arterial pressure is apparent (block 261), the increase is marked (block 262). If the increase in arterial pressure is followed by an overshoot (block 263), the overshoot is marked (block 264). For the Valsalva maneuver, the overshoot is the strongest trend indication in 10 the characteristic signature and indicates a healthy, non-heart failure person. If the overshoot is followed by a decrease in arterial pressure (block 265), the decrease is marked (block 266). Finally, if a resumption of normal arterial pressure is apparent (block 267), the resumption is marked (block 268).

Following the evaluation of each of the groups, the impedance measures 15 are correlated to cardiac stroke volume to reflect cardiac dimensional changes, as described above with reference to FIGURE 3. Next, the overall cardiac stroke volume profile 224 is determined (block 270) to generate a cardiac performance assessment 205. The cardiac performance assessment 205 quantifies the variants between the physiological measures determined during each of the phases against 20 the cardiac stroke volume profile trends 224e-224h. Following determination of the cardiac performance assessment 205, the routine returns.

In the described embodiment, the cardiac impedance data can be analyzed in several ways. In one embodiment, a statistical analysis can be performed on impedance data to determine the mean impedance level and standard deviation 25 over the entire response period. The mean \bar{Z} and the standard deviation S_z of the impedance data over the response period can be used as a cardiac performance assessment 205, where:

$$\bar{Z} = \frac{\sum Z_i}{n}$$

$$S_z = \sqrt{\frac{1}{N} \sum_{i=1}^N (Z_i - \bar{Z})^2}$$

In a further embodiment, a statistical analysis can be performed on different phases of the response period based on the collected impedance data to determine the cardiac performance assessment 205. For example, the mean and standard deviation analysis, described above, can be performed on physiological data from Phase IV of the response period relative to the performance of the Valsalva maneuver. The analyzed values reflect the amplitude of impedance change during the Valsalva maneuver as the cardiac performance assessment 205.

In a further embodiment, the impedance data can be analyzed for trends by calculating a linear regression over the collected data for Phase IV of the response period, such as described in Seborg et al., "Process Dynamics and Control," pp. 165-167 (John Wiley & Sons, 1989), the disclosure of which is incorporated by reference. By performing a linear regression, the response pattern during Phase IV can be fitted into a second-order system response, which is characterized by a transfer function, such as:

$$G(s) = \frac{K}{(\tau_1 s + 1)(\tau_2 s + 1)}$$

where τ_1 and τ_2 are derived empirically by linear regression. Alternatively, a second order process transfer function can arise upon transforming a second-order differential equation process model that has the general form of:

$$G(s) = \frac{K}{\tau^2 s^2 + 2\zeta\tau s + 1}$$

where ζ is the dimensionless damping factor.

By equating the two transfer functions, the value of the damping factor can be derived as:

$$\zeta = \frac{\tau_1 + \tau_2}{2\sqrt{\tau_1\tau_2}}$$

The resulting response pattern is characterized by the derived value of the damping factor ζ according to the following table:

$\zeta > 1$	Over damped
$\zeta = 1$	Critically damped

$0 < \zeta < 1$ Under damped

Phase IV of the Valsalva maneuver exhibits the most noticeable difference in cardiac response for the three groups of individuals described above with reference to FIGURES 3A-C and 4, that is, a healthy person, a patient suffering
5 from heart disease and a patient suffering from heart failure. During Phase IV, the response pattern from the healthy person group closely resembles an under-damped second-order response, which is characterized by a damping factor between zero and one. The response pattern from the heart disease patient group closely resembles a critically-damped or under-damped second-order response,
10 which is characterized by a damping factor that is equal to or greater than one but not substantially higher than one. The response pattern from the heart failure patient group shows no appreciable change, which resembles a severely-over damped system characterized by a large damping factor. The damping factor serves as a cardiac performance assessment 205. Other types of statistical
15 analyses can also be performed, as would be recognized by one skilled in the art.

While the invention has been particularly shown and described as referenced to the embodiments thereof, those skilled in the art will understand that the foregoing and other changes in form and detail may be made therein without departing from the spirit and scope of the invention.